

1647

OIPE

#12

RAW SEQUENCE LISTING

DATE: 09/07/2001

PATENT APPLICATION: US/09/600,991

TIME: 14:13:11

Input Set : A:\0471-0162P.ST25.txt

Output Set: N:\CRF3\09072001\I600991.raw

3 <110> APPLICANT: MEDICO, Enzo
 4 MICHELI, Paolo
 5 COLLESI, Chiara
 6 CASELLI, Gianfranco
 7 COMOGLIO, Paolo
 9 <120> TITLE OF INVENTION: RECOMBINANT PROTEINS DERIVED FROM HGF AND
 11 <130> FILE REFERENCE: 0471-0162P
 13 <140> CURRENT APPLICATION NUMBER: US 09/600,991
 C--> 14 <141> CURRENT FILING DATE: 2001-08-20
 16 <160> NUMBER OF SEQ ID NOS: 22
 18 <170> SOFTWARE: PatentIn version 3.1
 20 <210> SEQ ID NO: 1
 21 <211> LENGTH: 1725
 22 <212> TYPE: DNA
 23 <213> ORGANISM: Artificial Sequence
 25 <220> FEATURE:
 26 <223> OTHER INFORMATION: Magic F-1 DNA coding sequence
 28 <400> SEQUENCE: 1
 29 atgtgggtga ccaaactcct gccagccctg ctgctgcagc atgtcctcct gcatctcctc 60
 30 ctgctcccca tcgccatccc ctatgcagag ggacaaagga aaagaagaaa tacaattcat 120
 31 gaattcaaaa aatcagcaaa gactacccta atcaaaatag atccagcact gaagataaaa 180
 32 accaaaaaag tgaatactgc agaccaatgt gctaatagat gtactaggaa taaaggactt 240
 33 ccattcactt gcaaggcttt tgtttttgat aaagcaagaa aacaatgcct ctgggttccc 300
 34 ttcaatagca tgtcaagtgg agtgaaaaaa gaatttgagg atgaatttga cctctatgaa 360
 35 aacaaagact acattagaaa ctgcatcatt ggtaaaggac gcagctacaa ggaagacagta 420
 36 tctatcacta agagtggcat caaatgtcag ccctggagtt ccatgatacc acacgaacac 480
 37 agctatcggt gtaaagacct acaggaaaac tactgtcgaa atcctcgagg ggaagaaggg 540
 38 ggaccctggt gtttcacaag caatccagag gtacgcctacg aagtctgtga cattcctcag 600
 39 tgttcagaag ttgaatgcat gacctgcaat ggggagagtt atcgagggtc catggatcat 660
 40 acagaatcag gcaagatttg tcagcgctgg gatcatcaga caccacaccg gcacaaattc 720
 41 ttgcctgaaa gatataccga caagggtctt gatgataatt attgccgcaa tcccgatggc 780
 42 cagccgaggg catggtgcta tactcttgac cctcacaccc gctgggagta ctgtgcaatt 840
 43 aaaacatgcy ctgacaaagc ttggggcggt ggcggttctg gtggcggtgg ctccggcggt 900
 44 ggcggttctc tagaggggaca aaggaaaaga agaaatacaa ttcattgaatt caaaaaatca 960
 45 gcaaagacta ccctaataca aatagatcca gcactgaaga taaaaccaa aaaagtgaat 1020
 46 actgcagacc aatgtgctaa tagatgtact aggaataaag gacttcatt cacttgcaag 1080
 47 gcttttgttt ttgataaagc aagaaaacaa tgcctctggt tccccttcaa tagcatgtca 1140
 48 agtggagtga aaaaagaatt tggccatgaa tttgacctct atgaaaacaa agactacatt 1200
 49 agaaactgca tcattggtaa aggaacgcag tacaaggga cagtatctat cactaagagt 1260
 50 ggcatacaat gtcagccctg gagttccatg ataccacacg aacacagcta tcggggtaaa 1320
 51 gacctacagg aaaactactg tcgaaatcct cgagggggaag aagggggacc ctggtgtttc 1380
 52 acaagcaatc cagaggtacg ctacgaagtc tgtgacattc ctcagtgttc agaagttgaa 1440
 53 tgcattgacct gcaatgggga gagttatcga ggtctcatgg atcatacaga atcaggcaag 1500
 54 atttgtcagc gctgggatca tcagacacca caccggcaca aattcttgcc tgaaagatat 1560
 55 cccgacaagg gctttgatga taattattgc cgcaatcccg atggccagcc gagggcatgg 1620
 56 tgctatactc ttgacctca caccgcgtgg gactactgtg caattaaaac atgcgctgac 1680
 57 aaagctgacg acgacgacaa acaccaccac caccaccacc actag 1725

RECEIVED
 DEPT 1 2001
 TECH CENTER 1600/2900
 ENTERED

RAW SEQUENCE LISTING

DATE: 09/07/2001

PATENT APPLICATION: US/09/600,991

TIME: 14:13:11

Input Set.: A:\0471-0162P.ST25.txt

Output Set: N:\CRF3\09072001\I600991.raw

60 <210> SEQ ID NO: 2
 61 <211> LENGTH: 574
 62 <212> TYPE: PRT
 63 <213> ORGANISM: Artificial Sequence
 65 <220> FEATURE:
 66 <223> OTHER INFORMATION: Magic F-1 recombinant protein obtained combining hairpin loop
 and
 67 kringle domains of human HGF and MSP
 69 <400> SEQUENCE: 2
 71 Met Trp Val Thr Lys Leu Leu Pro Ala Leu Leu Leu Gln His Val Leu
 72 1 5 10 15
 74 Leu His Leu Leu Leu Leu Pro Ile Ala Ile Pro Tyr Ala Glu Gly Gln
 75 20 25 30
 77 Arg Lys Arg Arg Asn Thr Ile His Glu Phe Lys Lys Ser Ala Lys Thr
 78 35 40 45
 80 Thr Leu Ile Lys Ile Asp Pro Ala Leu Lys Ile Lys Thr Lys Lys Val
 81 50 55 60
 83 Asn Thr Ala Asp Gln Cys Ala Asn Arg Cys Thr Arg Asn Lys Gly Leu
 84 65 70 75 80
 86 Pro Phe Thr Cys Lys Ala Phe Val Phe Asp Lys Ala Arg Lys Gln Cys
 87 85 90 95
 89 Leu Trp Phe Pro Phe Asn Ser Met Ser Ser Gly Val Lys Lys Glu Phe
 90 100 105 110
 92 Gly His Glu Phe Asp Leu Tyr Glu Asn Lys Asp Tyr Ile Arg Asn Cys
 93 115 120 125
 95 Ile Ile Gly Lys Gly Arg Ser Tyr Lys Gly Thr Val Ser Ile Thr Lys
 96 130 135 140
 98 Ser Gly Ile Lys Cys Gln Pro Trp Ser Ser Met Ile Pro His Glu His
 99 145 150 155 160
 101 Ser Tyr Arg Gly Lys Asp Leu Gln Glu Asn Tyr Cys Arg Asn Pro Arg
 102 165 170 175
 104 Gly Glu Glu Gly Gly Pro Trp Cys Phe Thr Ser Asn Pro Glu Val Arg
 105 180 185 190
 107 Tyr Glu Val Cys Asp Ile Pro Gln Cys Ser Glu Val Glu Cys Met Thr
 108 195 200 205
 110 Cys Asn Gly Glu Ser Tyr Arg Gly Leu Met Asp His Thr Glu Ser Gly
 111 210 215 220
 113 Lys Ile Cys Gln Arg Trp Asp His Gln Thr Pro His Arg His Lys Phe
 114 225 230 235 240
 116 Leu Pro Glu Arg Tyr Pro Asp Lys Gly Phe Asp Asp Asn Tyr Cys Arg
 117 245 250 255
 119 Asn Pro Asp Gly Gln Pro Arg Pro Trp Cys Tyr Thr Leu Asp Pro His
 120 260 265 270
 122 Thr Arg Trp Glu Tyr Cys Ala Ile Lys Thr Cys Ala Asp Lys Ala Ser
 123 275 280 285
 125 Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Leu
 126 290 295 300
 128 Glu Gly Gln Arg Lys Arg Arg Asn Thr Ile His Glu Phe Lys Lys Ser
 129 305 310 315 320
 131 Ala Lys Thr Thr Leu Ile Lys Ile Asp Pro Ala Leu Lys Ile Lys Thr

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/600,991

DATE: 09/07/2001

TIME: 14:13:11

Input Set : A:\0471-0162P.ST25.txt

Output Set: N:\CRF3\09072001\I600991.raw

```

132          325          330          335
134 Lys Lys Val Asn Thr Ala Asp Gln Cys Ala Asn Arg Cys Thr Arg Asn
135          340          345          350
137 Lys Gly Leu Pro Phe Thr Cys Lys Ala Phe Val Phe Asp Lys Ala Arg
138          355          360          365
140 Lys Gln Cys Leu Trp Phe Pro Phe Asn Ser Met Ser Ser Gly Val Lys
141          370          375          380
143 Lys Glu Phe Gly His Glu Phe Asp Leu Tyr Glu Asn Lys Asp Tyr Ile
144 385          390          395          400
146 Arg Asn Cys Ile Ile Gly Lys Gly Arg Ser Tyr Lys Gly Thr Val Ser
147          405          410          415
149 Ile Thr Lys Ser Gly Ile Lys Cys Gln Pro Trp Ser Ser Met Ile Pro
150          420          425          430
152 His Glu His Ser Tyr Arg Gly Lys Asp Leu Gln Glu Asn Tyr Cys Arg
153          435          440          445
155 Asn Pro Arg Gly Glu Glu Gly Gly Pro Trp Cys Phe Thr Ser Asn Pro
156          450          455          460
158 Glu Val Arg Tyr Glu Val Cys Asp Ile Pro Gln Cys Ser Glu Val Glu
159 465          470          475          480
161 Cys Met Thr Cys Asn Gly Glu Ser Tyr Arg Gly Leu Met Asp His Thr
162          485          490          495
164 Glu Ser Gly Lys Ile Cys Gln Arg Trp Asp His Gln Thr Pro His Arg
165          500          505          510
167 His Lys Phe Leu Pro Glu Arg Tyr Pro Asp Lys Gly Phe Asp Asp Asn
168          515          520          525
170 Tyr Cys Arg Asn Pro Asp Gly Gln Pro Arg Pro Trp Cys Tyr Thr Leu
171          530          535          540
173 Asp Pro His Thr Arg Trp Glu Tyr Cys Ala Ile Lys Thr Cys Ala Asp
174 545          550          555          560
176 Lys Ala Asp Asp Asp Asp Lys His His His His His His His
177          565          570

```

180 <210> SEQ ID NO: 3

181 <211> LENGTH: 1692

182 <212> TYPE: DNA

183 <213> ORGANISM: Artificial Sequence

185 <220> FEATURE:

186 <223> OTHER INFORMATION: Metron F-1 DNA coding sequence

188 <400> SEQUENCE: 3

```

189 atgggggtggc tccactcct gctgcttctg actcaatgct taggggtccc tgggcagcgc      60
190 tcgccattga atgacttcca agtgctccgg ggcacagagc tacagcacct gctacatgcg      120
191 gtgggtgcccg ggccttggca ggaggatgtg gcagatgctg aagagtgtgc tggtcgctgt      180
192 gggcccttaa tggactgccg ggccttccac tacaacgtga gcagccatgg ttgccaaactg      240
193 ctgccatgga ctcaacactc gccccacacg aggctgcggc gttctgggcg ctgtgacctc      300
194 ttccagaaga aagactacgt acggacctgc atcatgaaca atggggttgg gtaccggggc      360
195 accatggcca cgaccgtggg tggcctgccc tgccaggctt ggagccacaa gttcccgaat      420
196 gatcacaagt acacgcccac tctccggaat ggcctggaag agaacttctg ccgtaaccct      480
197 gatggcgacc cgggaggtcc ttggtgctac acaacagacc ctgctgtgcg cttccagagc      540
198 tgcggcatca aatcctgccg ggaggccgcg tgtgtctggt gcaatggcga ggaataccgc      600
199 ggcgcggtag accgcacgga gtcaggggcg gagtgccagc gctgggatct tcagcacccg      660

```

RAW SEQUENCE LISTING

DATE: 09/07/2001

PATENT APPLICATION: US/09/600,991

TIME: 14:13:11

Input Set : A:\0471-0162P.ST25.txt

Output Set: N:\CRF3\09072001\I600991.raw

```

200 caccagcacc ccttcgagcc gggcaagttc ctcgaccaag gtctggacga caactattgc 720
201 cggaatcctg acggctccga gcggccatgg tgctacacta cggatccgca gatcgagcga 780
202 gagttctgtg acctcccccg ctgcgggtcc gaggcacagc cccgcctcga gggcggtggc 840
203 ggttctggtg gcgggtggctc cggcggtggc ggttctctag agggacaaag gaaaagaaga 900
204 aatacaattc atgaattcaa aaaatcagca aagactacc taatcaaat agatccagca 960
205 ctgaagataa aaacaaaaaa agtgaatact gcagaccaat gtgctaatag atgtactagg 1020
206 aataaaggac ttccattcac ttgcaaggct tttgtttttg ataaagcaag aaaacaatgc 1080
207 ctctggttcc ctttcaatag catgtcaagt ggagtgaata aagaatttgg ccatgaattt 1140
208 gacctctatg aaaacaaaga ctacattaga aactgcatca ttggtaaagg acgcagctac 1200
209 aaggggaacag tatctatcac taagagtggc atcaaagtgc agccctggag ttccatgata 1260
210 ccacacgaac acagctatcg gggtaaagac ctacaggaaa actactgtcg aaatcctcga 1320
211 ggggaagaag ggggaccctg gtgtttcaca agcaatccag aggtacgcta cgaagtctgt 1380
212 gacattcctc agtgttcaga agttgaatgc atgacctgca atggggagag ttatcgaggt 1440
213 ctcatggatc atacagaatc aggcaagatt tgcagcgcgt gggatcatca gacaccacac 1500
214 cggcacaaat tcttgccctga aagatatccc gacaagggct ttgatgataa ttattgccgc 1560
215 aatcccgatg gccagccgag gccatgggtgc tatactcttg accctcacac ccgctgggag 1620
216 tactgtgcaa ttaaaacatg cgctgacaaa gctgacgacg acgacaaaca ccaccaccac 1680
217 caccaccact ag 1692

```

220 <210> SEQ ID NO: 4

221 <211> LENGTH: 563

222 <212> TYPE: PRT

223 <213> ORGANISM: Artificial Sequence

225 <220> FEATURE:

226 <223> OTHER INFORMATION: Metron F-1 recombinant protein obtained combining hairpin
loop and

227 kringle domains of human HGF and MSP

229 <400> SEQUENCE: 4

```

231 Met Gly Trp Leu Pro Leu Leu Leu Leu Leu Thr Gln Cys Leu Gly Val
232 1 5 10 15
234 Pro Gly Gln Arg Ser Pro Leu Asn Asp Phe Gln Val Leu Arg Gly Thr
235 20 25 30
237 Glu Leu Gln His Leu Leu His Ala Val Val Pro Gly Pro Trp Gln Glu
238 35 40 45
240 Asp Val Ala Asp Ala Glu Glu Cys Ala Gly Arg Cys Gly Pro Leu Met
241 50 55 60
243 Asp Cys Arg Ala Phe His Tyr Asn Val Ser Ser His Gly Cys Gln Leu
244 65 70 75 80
246 Leu Pro Trp Thr Gln His Ser Pro His Thr Arg Leu Arg Arg Ser Gly
247 85 90 95
249 Arg Cys Asp Leu Phe Gln Lys Lys Asp Tyr Val Arg Thr Cys Ile Met
250 100 105 110
252 Asn Asn Gly Val Gly Tyr Arg Gly Thr Met Ala Thr Thr Val Gly Gly
253 115 120 125
255 Leu Pro Cys Gln Ala Trp Ser His Lys Phe Pro Asn Asp His Lys Tyr
256 130 135 140
258 Thr Pro Thr Leu Arg Asn Gly Leu Glu Glu Asn Phe Cys Arg Asn Pro
259 145 150 155 160
261 Asp Gly Asp Pro Gly Gly Pro Trp Cys Tyr Thr Thr Asp Pro Ala Val
262 165 170 175
264 Arg Phe Gln Ser Cys Gly Ile Lys Ser Cys Arg Glu Ala Ala Cys Val

```

RAW SEQUENCE LISTING

DATE: 09/07/2001

PATENT APPLICATION: US/09/600,991

TIME: 14:13:11

Input Set : A:\0471-0162P.ST25.txt

Output Set: N:\CRF3\09072001\I600991.raw

```

265          180          185          190
267 Trp Cys Asn Gly Glu Glu Tyr Arg Gly Ala Val Asp Arg Thr Glu Ser
268          195          200          205
270 Gly Arg Glu Cys Gln Arg Trp Asp Leu Gln His Pro His Gln His Pro
271          210          215          220
273 Phe Glu Pro Gly Lys Phe Leu Asp Gln Gly Leu Asp Asp Asn Tyr Cys
274 225          230          235          240
276 Arg Asn Pro Asp Gly Ser Glu Arg Pro Trp Cys Tyr Thr Thr Asp Pro
277          245          250          255
279 Gln Ile Glu Arg Glu Phe Cys Asp Leu Pro Arg Cys Gly Ser Glu Ala
280          260          265          270
282 Gln Pro Arg Leu Glu Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
283          275          280          285
285 Gly Gly Gly Ser Leu Glu Gly Gln Arg Lys Arg Arg Asn Thr Ile His
286          290          295          300
288 Glu Phe Lys Lys Ser Ala Lys Thr Thr Leu Ile Lys Ile Asp Pro Ala
289 305          310          315          320
291 Leu Lys Ile Lys Thr Lys Lys Val Asn Thr Ala Asp Gln Cys Ala Asn
292          325          330          335
294 Arg Cys Thr Arg Asn Lys Gly Leu Pro Phe Thr Cys Lys Ala Phe Val
295          340          345          350
297 Phe Asp Lys Ala Arg Lys Gln Cys Leu Trp Phe Pro Phe Asn Ser Met
298          355          360          365
300 Ser Ser Gly Val Lys Lys Glu Phe Gly His Glu Phe Asp Leu Tyr Glu
301          370          375          380
303 Asn Lys Asp Tyr Ile Arg Asn Cys Ile Ile Gly Lys Gly Arg Ser Tyr
304 385          390          395          400
306 Lys Gly Thr Val Ser Ile Thr Lys Ser Gly Ile Lys Cys Gln Pro Trp
307          405          410          415
309 Ser Ser Met Ile Pro His Glu His Ser Tyr Arg Gly Lys Asp Leu Gln
310          420          425          430
312 Glu Asn Tyr Cys Arg Asn Pro Arg Gly Glu Glu Gly Gly Pro Trp Cys
313          435          440          445
315 Phe Thr Ser Asn Pro Glu Val Arg Tyr Glu Val Cys Asp Ile Pro Gln
316          450          455          460
318 Cys Ser Glu Val Glu Cys Met Thr Cys Asn Gly Glu Ser Tyr Arg Gly
319 465          470          475          480
321 Leu Met Asp His Thr Glu Ser Gly Lys Ile Cys Gln Arg Trp Asp His
322          485          490          495
324 Gln Thr Pro His Arg His Lys Phe Leu Pro Glu Arg Tyr Pro Asp Lys
325          500          505          510
327 Gly Phe Asp Asp Asn Tyr Cys Arg Asn Pro Asp Gly Gln Pro Arg Pro
328          515          520          525
330 Trp Cys Tyr Thr Leu Asp Pro His Thr Arg Trp Glu Tyr Cys Ala Ile
331          530          535          540
333 Lys Thr Cys Ala Asp Lys Ala Asp Asp Asp Asp Lys His His His His
334 545          550          555          560
336 His His His
340 <210> SEQ ID NO: 5

```

VERIFICATION SUMMARY

DATE: 09/07/2001

PATENT APPLICATION: US/09/600,991

TIME: 14:13:12

Input Set : A:\0471-0162P.ST25.txt

Output Set: N:\CRF3\09072001\I600991.raw

L:14 M:271 C: Current Filing Date differs, Replaced Current Filing Date